

REMARKS

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the changes place the application in condition for allowance.

I. Status of the Claims and Formal Matters

Claims 1-20 and 23 are under examination in this application. Claims 14 and 20 have been amended, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. New claims 24-25 have been added. No new matter has been added by these amendments.

Support for these amendments is found throughout the specification. The recitation of a duration of electromagnetic energy of at least five minutes is found in the Detailed Description (page 10) of the specification as originally filed.

The Examiner is thanked for withdrawing the 35 U.S.C. § 102(e) rejection of the Murphy and Melke references.

Claims 1, 14 and 20 have been amended without prejudice, without admission, and without surrender of subject matter, and without any intention of creating any estoppel as to equivalents to recite the base claim and intervening claims.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. The Rejections Under 35 U.S.C. § 112 (second paragraph) are overcome

The Office Action rejected claims 14 and 18 for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner alleges that LASIK is a trademark and is used in claims 14 and 20 as a limitation to identify or describe a particular product.

Although the Applicants do not agree with the Examiner, in the interest of expediting prosecution, claims 14 and 20 have been clarified to delete the recitation of “LASIK”, thereby obviating the rejection.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112 (second paragraph) are respectfully requested.

III. The Rejections Under 35 U.S.C. § 102(b) are overcome

The Office Action rejected claims 1-14, 17-20 and 23 as allegedly being anticipated by Khadem (U.S. Patent No. 5,552,452). The Office Action asserts that the Khadem discloses a method for adhering tissue comprising: contacting a tissue with a photosensitizer, creating a tissue-photosensitizer complex, applying electromagnetic energy without more than a 1 degree rise in temperature, and creating a tissue seal without contacting the tissue with an exogenous cross-linkable substrate.

This rejection is respectfully traversed. The limited description provided in the specification of Khadem is not enabling for methods of creating a tissue seal in the absence of an exogenous cross-linkable substrate.

The prior art must contain an enabling disclosure for a Section 102 rejection to stand. *See Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). “A claimed reference cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.” *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003).

A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See, e.g., Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003) and *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). “The disclosure must be such as will give possession of the invention to the person of ordinary skill. Even the act of publication or the fiction of constructive reduction to practice will not suffice if the disclosure does not meet this standard.” *See In re Borst*, 52 C.C.P.A. 1398, 345 F.2d 851, 855, 145 USPQ 554, 557 (CCPA 1962).

This rejection is respectfully traversed. The limited description provided in the specification of Khadem is not enabling for methods of creating a tissue seal in the absence of an

exogenous cross-linkable substrate. In this regard, the specification of Khadem, at column 7 lines 18-30 (emphasis added), teaches only as follows:

“The present invention also encompasses methods for tissue closing or wound healing wherein the actual preparation of a separate protein or peptide containing composition is not necessary. Such methods utilize the peptides or proteins located naturally within the tissue area as in situ protein containing compositions. To form an adhesive connection between biological tissues in this manner one would form a biologically effective amount of a tissue adhesive combination at the tissues **by applying only the photosensitizer component to the tissues**. One would then again apply electromagnetic radiation the tissue adhesive combination thus formed in a manner effective to promote the formation of an adhesive connection between the tissues.”

As is apparent from this limited description:

- Khadem provides no teaching of specific tissues for which tissue adherence in the absence of an exogenous cross-linkable substrate will be effective;
- Khadem provides no teaching of specific photosensitizers (or excitation wavelengths thereof) that will be effective in such methods; and
- Khadem provides no exemplification of means creating a tissue seal without contacting the tissue with an exogenous cross-linkable substrate. None of the Examples in Khadem demonstrate that a tissue seal can be formed without administration of an exogenous cross-linkable substrate.

Thus, Khadem provides no reasonable expectation of success for methods of producing a tissue seal without administration of an exogenous cross-linkable substrate.

The remaining disclosure in Khadem cannot be extended to methods of producing a tissue seal without administration of an exogenous cross-linkable substrate. For example, Khadem states that its methods can be applied to a variety of tissues including the cornea and other tissues of the eye (column 8 line 29 and Example 8) and that the photosensitizer can be methylene blue (column 4 line 64-66). As can be seen from Example 5 of the present application, the photosensitizer methylene blue is not effective in repair of corneal lesions. Therefore, the teaching of Khadem in its entirety encompasses methods that are not operable.

In summary, the above-referenced statements in Khadem—which amount to no more than four sentences—are not enabled and thus fail to provide any reasonable expectation of

success for methods of producing a tissue seal without administration of an exogenous cross-linkable substrate.

Submitted herewith is a Declaration of Michael R. Hamblin Ph.D. Under 37 C.F.R. § 1.132 (“the Declaration”) relating to the lack of enablement of the Khadem disclosure as it pertains to a method of adhering tissue in the absence of an exogenous cross-linkable substrate. The declarant, Professor Hamblin, is not an Applicant of the present application. Applicants respectfully request that the enclosed Declaration be accepted as evidence regarding the enablement of the Khadem disclosure as it relates to a method of adhering tissue in the absence of an exogenous peptide or protein.

Professor Hamblin’s *Curriculum vitae* is attached to the Declaration. Professor Hamblin is considered by his peers to be an expert in the field to which the present application pertains. Accordingly, it is respectfully submitted that Professor Hamblin can provide expert opinions and facts with respect to that which is disclosed and enabled by the present invention and related fields, including Khadem.

The accompanying Declaration is made in response to the assertion in the Office Action that Khadem discloses a method for adhering tissue comprising: contacting a tissue with a photosensitizer, creating a tissue-photosensitizer complex, applying electromagnetic energy without more than a 1 degree rise in temperature, and creating a tissue seal without contacting the tissue with an exogenous cross-linkable substrate.

A prior art reference contains an enabling disclosure if a person of ordinary skill could have combined the description of the invention in the prior art reference with his own knowledge of the art to place himself in possession of the invention. According to Professor Hamblin, Khadem does not meet this standard because Khadem does not teach a person of ordinary skill in the art how to create a tissue seal in the absence of an exogenous cross-linkable substrate. In Professor Hamblin’s expert opinion, Khadem does not provide one of ordinary skill in the art with the necessary disclosure to combine the Khadem description with his own knowledge to practice the presently claimed invention.

Accordingly, claims 1-2, 4-8 and 11-14 are not anticipated by Khadem because Khadem is not prior art. Khadem does not contain enabling disclosure with respect to creating a tissue seal without contacting the tissue with an exogenous cross-linkable substrate.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 102 are respectfully requested.

IV. The Rejections Under 35 U.S.C. § 103(a) are Overcome

Claims 15 and 16 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Khadem. The Office Action alleges that Khadem discloses a method for adhering tissue comprising: contacting a tissue with a photosensitizer, creating a tissue-photosensitizer mixture, applying electromagnetic energy without more than a 1 degree rise in temperature, however Khadem fails to disclose specific W/cm and J/cm ranges. The Examiner contends that it would have been obvious to one of ordinary skill in the art to combine the teaching with routine experimentation to determine the optimum ranges of energy doses and irradiances, to a method for adhering tissue as per Khadem in order to minimize tissue damage.

This rejection is respectfully traversed. As discussed above, the limited description provided in the specification of Khadem is not enabling for methods of creating a tissue seal in the absence of an exogenous cross-linkable substrate. Accordingly, when viewed under § 103, the teaching of Khadem does not provide adequate guidance for one of ordinary skill to engage in routine experimentation to determine the optimum ranges of energy doses and/or irradiances in order to practice the presently claimed invention.¹ In view of Khadem, one skilled in the art would have no reasonable expectation of success in practicing the claimed methods. *See In re Vaack*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1988). Khadem is therefore no more effective as a citation under 35 U.S.C. § 103 as it is under 35 U.S.C. § 102. Khadem does not enable, teach or suggest the present invention.

Moreover, whatever guidance Khadem does provide relates solely to use of a cross-linkable substrate, and therefore, does not teach or suggest the improvements of the present invention. Methods for adhering tissues with an exogenous cross-linkable substrate are disadvantageous for several reasons. First, the exogenous cross-linkable substrate is a filler material that creates gaps when added to the tissue and subsequently cross-linked. These gaps can fill with fibrotic material, therefore resulting in inflammation and scar formation. Second,

¹ Under § 103, a reference that is not enabled nonetheless qualifies as prior art for what it discloses. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1357 (Fed. Cir. 2003).

the exogenous material that is not native to the tissue forms an amorphous bridge between tissues that must be remodeled by the body. Such tissue remodeling can also result in inflammation and scar formation. Third, any time an exogenous material is added to a tissue, the regular structure of the tissue is lost, which can also result in inflammation and scar formation.

Accordingly, the presently claimed invention is an improvement over methods for adhering tissues with an exogenous cross-linkable substrate. Since a photosensitizer is added without an exogenous cross-linkable substrate, complications, such inflammation and scar formation that can result from gap formation, tissue remodeling and loss of regular tissue structure in the presence of such a substrate, are significantly reduced.

Applicants respectfully point out that the presently claimed invention pertains to use of a longer wavelength (i.e., greater than about 488 nm) for a longer duration (i.e., at least five minutes) that results in better penetration, which in turn produces longitudinal bonding within a target tissue. Tissues bonded according to the claimed methods have greater strength after bonding and are not subject to thermal damage.

Thus, methods of the present invention are not only distinct, but also superior in comparison to the methods of the cited reference.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the amendments and remarks herewith, the application is in condition for allowance. Favorable reconsideration of the application, reconsideration, and withdrawal of the objections to and rejections of the application, and prompt issuance of a Notice of Allowance are respectfully requested.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: Deborah L. Lu
Thomas J. Kowalski
Reg. No. 32,147
Amy Leahy
Reg. No. 47,739
Deborah L. Lu
Reg. No. 50,940
(212) 588-0800
(212) 588-0500 (facsimile)